

Appl. No. 09/643,755  
Amdt. Dated May 27, 2004  
Reply to Office action of December 16, 2003

#### **REMARKS/ARGUMENTS**

By the present amendment, claims 1, 17, 21 and 22 have been amended and claims 18-20 have been deleted. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicant reserves the right to pursue any of the deleted subject matter in a further continuation, continuation-in-part or divisional application. The amendment does not contain new matter and its entry is respectfully requested.

The Official Action dated December 16, 2003 has been carefully considered. It is believed that the amended specification and the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

#### **35 U.S.C. §102**

The Examiner has objected to claims 1, 3, 5-7, 11 and 13-19 under 35 U.S.C. 102(b) as being anticipated by Willmitzer et al. (WO 92/01042).

By the present amendment, independent claims 1 and 17 have been amended in order to incorporate the subject matter of previous claim 20 which has been deleted. We note that previous claim 20 was not under objection and therefore amended claims 1 and 17 and the claims dependent thereon are novel. In particular, Willmitzer does not disclose the method of isolating chymosin from plant seed as described in step (d) of these claims.

In view of the foregoing, we respectfully request that the objections to the claims under 35 U.S.C. 102 (b) be withdrawn.

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**35 U.S.C. §103**

The Examiner has objected to claims 1-8, 10, 11 and 13-23 under 35 USC §103(a) as being unpatentable over Willmitzer et al. and further in view of Applicant's admitted prior art.

As mentioned above, the independent method claims 1 and 17 have now been amended in order to include steps for isolating the chymosin from the plant seed. The steps involve fractionating crushed seed into an oil fraction, an aqueous fraction and a fraction comprising insoluble material and then subsequently contacting the aqueous fraction containing the chymosin with a protein binding resin. None of these steps are disclosed or suggested in Willmitzer. Further, one of skill in the art would not be motivated to include such steps having read Willmitzer for the following reasons.

First, as Willmitzer does not prepare chymosin in seed, Willmitzer does not isolate chymosin from seed. Willmitzer uses a constitutive promoter which results in the expression of chymosin in various plant parts and Willmitzer isolates the chymosin from the leaves. Second, Willmitzer does not prepare chymosin in plants containing high levels of oil. Willmitzer only works in tobacco and potato plants. Consequently, Willmitzer would provide no motivation for one of skill in the art to develop methods to isolate chymosin from oil seeds.

At the time that the invention, recombinant proteins had been prepared in oil seeds. However, the purification of recombination proteins from oil seeds was difficult due to the presence of large quantities of oil which would make the subsequent purification steps problematic. The art-recognized solution to the problem was to extract the oil using conventional hexane extraction procedures. However, the use of hexane or other organics solvents to extract proteins was not desirable due to the denaturant property of such solvents. We are enclosing a paper by Cramer et al. (*Current Topics in Microbiology and Immunology*, Vol. 240, p. 95-118, 1999) which states at page 107 that

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"methods of efficiently recovering proteins from the apoplastic fluid have yet to be developed".

The problems of the prior art were solved by the present invention. In particular, the present inventors determined that chymosin could be recovered by fractionating the crushed plant seed into an oil fraction, an aqueous fraction and a fraction comprising insoluble material using an aqueous extraction protocol. Organic solvents are not required which overcomes the disadvantages of the prior art.

In view of the above, the claims of the present invention are inventive over Willmitzer as Willmitzer provides no disclosure, suggestion or motivation to isolate the chymosin from plant seeds using aqueous extraction. We do not understand the Examiner's statement on page 7 of the office action that states that "Willmitzer teaches methods of protein isolation using a protein binding resin". Respectfully, we cannot find any disclosure in Willmitzer that relates to the use of a protein binding resin.

In support of the inventiveness of the claims, we enclose a Declaration under 37 CFR §1.132, executed by Dr. David Dennis, a plant biochemist who is the President and CEO of a plant biotechnology company, Performance Plants Inc. Dr. Dennis declares that the preparation and isolation of chymosin as specified in the amended claims is not obvious in light of Willmitzer. Dr. Dennis is a person of skill in the area of the invention and is a disinterested third party to the Applicant.

The Examiner has also objected to claims 1-8 and 10-23 under 35 USC §103(a) as being unpatentable over Willmitzer and further in view of Adang et al. (U.S. 5,380,831).

As mentioned previously, the independent claims have now been amended in order to include steps for isolating the chymosin from the seed. The claims are clearly inventive over Willmitzer for the reasons stated above. The deficiencies in Willmitzer are in no way remedied by Adang as Adang is not concerned with methods of preparing

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chymosin in plant seeds and with methods of isolating the chymosin from the plant seeds.

In view of the foregoing, we respectfully request that all of the objections to the claims under 35 U.S.C. §103(a) be withdrawn.

The Commissioner is hereby authorized to charge any deficiency in fees (including any claim fees) or credit any overpayment to our Deposit Account No. 02-2095.

In view of the foregoing, we submit that the application is in order for allowance and an early indication to that effect would be greatly appreciated.

Respectfully submitted,

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Attachments